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Videoconference vs. Face-to-Face Delivery of Behavior Therapy for Youths with Tourette Syndrome in the Time of COVID-19: Follow-up over 6 months.

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INDICE

Abstract

Background: Tourette Syndrome (TS) a childhood-onset neurodevelopmental disorder with a worldwide prevalence of about 0.3–1% of the population. Research studies have explored the possible benefits of digital health interventions (DHIs) for the treatment of neurodevelopmental disorders, including tics and associated comorbidities, especially in the time of COVID-19 global pandemic.

Objective: To evaluate the phenomenology and course of a cohort of TS patients, treated with online remote behavior therapy, compared with face-to-face behavior therapy.

Methods: Data were collected to investigate the course and phenomenology of patients' tics, presence of comorbidities, overall treatment approaches. Among the clinical cohort, modifications in symptoms severity were further evaluated at 6-month follow-up, through the administration of Yale Global Tic Severity Rating Scale (YGTSS), Premonitory Urge for Tic Scale (PUTS), Children's Yale-Brown Obsessive-Compulsive Scale for Children (CY-BOCS), Multidimensional Anxiety Scale for Children (MASC), Child Depression Inventory (CDI), and the Conners' Parent Rating Scale (CPRS).

Results: Online remote and face-to-face behavior therapy are both effective in the treatment of tics and co-occurring disorders. Both groups showed an improvement in the severity of tics and associated symptoms, as assessed by neuropsychological findings. This improvement persisted over time, at least until the end of the follow-up period (6 months).

Conclusions: This study suggest that online remote behavior therapy is a promising and effective tool for patients affected by tic disorders. Despite this findings, further studies are needed to compare this alternative treatment option to traditional face-to-face care.

1. INTRODUCTION

1.1. Background

Tourette syndrome (TS), also known as Gilles de la Tourette syndrome or Tourette disorder, is a complex, childhood-onset neuropsychiatric condition that includes multiple motor and vocal tics with duration of at least 1 year, during which a tic-free period cannot past longer than 3 consecutive months (American Psychiatric Association, 2013). According to the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5) tics are defined as sudden, rapid, recurrent, nonrhythmic motor movements or vocalizations usually appearing in bouts while waxing and waning in frequency, intensity, and kind of tics (American Psychiatric Association, 2013). The prevalence of TS in young people was even estimated to be approximately 1% (Robertson, 2015; Scharf et al., 2015). TS have a strong male predominance, with a male-to-female ratio of about 4:1 (Knight et al., 2012). Tics usually begin between the age of 4-6 years, increase in severity into early adolescence, and can also persist into adulthood and, in some cases, can be severe and debilitating (Bloch & Leckman, 2009). Co-occurring comorbid disorders including attention deficit/hyperactivity disorder (ADHD), obsessive-compulsive disorder (OCD), autism spectrum disorders (ASD), learning disabilities (LD), or other psychopathologies are common among individuals with tic disorders (Hirschtritt et al., 2015; Rizzo et al., 2017). Tics and co-occurring conditions are associated with functional impairment and contribute to affect health-related quality of life (Eddy et al., 2011; Rizzo et al., 2014). For this reason, a prompt diagnosis and characterisation of comorbidities in TS patients is more important, particularly for a clear definition of therapeutic approaches. The etiology of TS is complex and multifactorial. TS is polygenic, involving multiple common risk variants combined with rare, inherited or de novo mutations. TS has a complex inheritance pattern and, according to several genome-wide association studies,

various genes and loci have been correlated with TS (Lin et al., 2022). Furthermore, recent studies have shown that Copy Number Variations (CNVs), which are polymorphisms in the number of gene copies due to chromosomal deletions or duplications, are considered another important source of mutations in TS (Saia et al., 2023). In general, TS is a heterogeneous disorder in which the phenotypic expression may be affected by non-genetic factors, including environmental factors such as perinatal events, smoking during pregnancy (Ayubi et al., 2021), and immune-mediated mechanisms including microglial dysfunction, reduced numbers of regulatory T cells, altered gamma globulin, and an increased response to pathogens (Martino et al., 2015; Singer, 2019). Although the pathophysiology of TS is not well understood, functional neuroimaging studies have revealed the role of a dysregulation of corticostriato-thalamo-cortical (CSTC) networks as a widely accepted pathophysiological substrate in tic disorders (Hsu et al., 2020).

1.2. Treatment options

The management of TS is a challenge for clinicians, given the high interindividual variability of tics and the possible association with comorbid conditions that may interfere with the treatment effects for symptoms. Based on the European clinical guidelines for TS and other tic disorders, psychological intervention has been recommended as the first line treatment, and behaviour therapy (BT) as a first-line intervention when psychoeducation alone is insufficient (Andrén et al., 2022a). Two approaches, habit reversal training (HRT; and its expanded version, Comprehensive Behavioral Intervention for Tics; CBIT) and exposure with response prevention (ERP), have ghatered the strongest evidence. (Piacentini & Chang, 2006; Rizzo et al., 2018; Andrén et al.,

2022a). Both interventions are considered first line behavioural treatments for tics for children and adults and should be offered to a patient, considering his preference (Andrén et al., 2022a). In situations where BT are ineffective, not available, not age-appropriate, or not the patient's or the family's preference, then pharmacological treatments should be considered, alone or in combination with BT. Among pharmacological options, the largest amount of evidence was found for dopamine blocking agents, preferably aripiprazole because of a more favourable profile of adverse events than first- and second-generation antipsychotics (Roessner et al., 2021). Other drugs that can be considered include risperidone, tiapride, and especially in case of comorbid ADHD, clonidine and guanfacine (Roessner et al., 2021). Furthermore, each pharmacological option is commonly associated with potential adverse effects including sedation, extrapyramidal effects, weight gain or cardiac risks, that are scarcely tolerated by patients and can lead to a discontinuation of drug use. Thus, while pharmacotherapy and BT are effective interventions for tics, there are still a significant number of TS patients who do not tolerate or benefit from these methods of treatment.

1.3. The Impact of the COVID-19 pandemic and lockdown on Children with Tic Disorders

Since the start of the COVID-19 global pandemic, lockdown and subsequent social isolations have impacted on the mental health of children and adolescents. During the pandemic, children and young people had experienced a markedly different social context, due to the lockdown measures put in place worldwide by health authorities to reduce viral circulation (Rizzo et al., 2021; Esposito et al., 2022). Preliminary results have showed a severe impairment of the mental health of young people, including an increase in internalizing symptoms, particularly anxiety, depression and eating disorders (Magson

et al., 2021; Bera et al., 2022; Doyle et al., 2022). Research studies focusing on the observed impact of COVID-19 have indicated that development of mental health dysfunctions was found more common in adolescents, in females, and in patients with previously diagnosed neuropsychiatric conditions (Bova et al., 2021; Esposito et al., 2021). Already, research data suggested that children and adolescents with pre-existing neuropsychiatric concerns may be vulnerable to psychiatric and psychosocial difficulties (Doyle et al., 2022). However, limited studies have explored the impact of lockdown on children with specific neuropsychiatric conditions, such as tic disorders, with conflicting results. In a study conducted in Italy during the early stages of the COVID-19 lockdown, it was reported a considerable impact on the mental health of young individuals with TS by worsening both tics and emotional and behavioral symptoms (Conte et al., 2020). During the COVID-19 pandemic, perceived changes in tic severity, as well as restlessness and irritability, were also described in school-age patients affected by tic disorders (Termine et al., 2022). Conversely, a prospective cohort study explored the impact of COVID-19 pandemic on tic symptoms in children and young people, showing no significant differences in tic symptom or severity between participants who were assessed before and during COVID-19 (Hall et al., 2022). In addition, during the global pandemic caused by COVID-19, it was reported a dramatic increase in functional tic-like behaviors in vulnerable children and adolescents after social media exposure (Paulus et al., 2021; Han et al., 2022), and also in patients with a previous diagnosis of tic disorder (Prato et al., 2023). To date, evaluation and management of TS require frequent travel to tertiary centers and multiple longitudinal in-person visits (Cen et al., 2020). During the global pandemic, the access to health services for patients with tic disorders was dramatically reduced by the patients' locations and the sparse availability of specific behaviour treatments for tics. Recent studies have explored the benefits of delivering treatment in

an intensive and brief manner, potentially making treatment more efficient and convenient for patients who travel long distances to receive care (Andrén et al., 2022a). In fact, a promising development in increasing accessibility to behavioural treatments has been the use of digital health interventions (DHIs), especially in the time of COVID pandemic (Hollis et al., 2021). Research studies suggested the effectiveness of DHIs for the treatment of children and young people with tic disorders (Ricketts et al., 2016; Andrén et al., 2019; Khan et al., 2020). Considering the major feasibility of this kind of interventions, tele-health could be an innovative and particularly attractive approach for the management of TS patients, likely beyond the end of the COVID-19 pandemic. Notably, although virtual treatment approaches had multiple advantages, there are also several limitations including technological difficulties such as internet availability, connection reliability, and sound and video quality that can negatively impact treatment (Woods et al., 2023).

1.4. Aim of the study

In 2022, we published a pilot study conducted on a small cohort of TS patients seen at the Child and Adolescent Neurology and Psychiatry of the Medical and Experimental Department of Catania University (Prato et al., 2022). In this pilot study, we compared the efficacy of online remote BT (or-BT, n=20) vs. face-to-face BT (ftf-BT, n=20) in reducing tics and associated comorbidities, through the evaluation of changes in symptom severity by the difference in the rating scales between the baseline (T0) and after two months (T1). BT was conducted remotely or face-to-face, according to the therapist manual developed by Verdellen et al. (2011). In detail, either HRT or ERP were conducted over eight weekly sessions, and sessions were 60 minutes in length. To perform

or-BT was used Skype©, a remote communication software application providing free web-based videoconferencing and utilizing security features (including standard encryption algorithms and digital user authentication certificates). Treatment was delivered from a private clinic room, using a desktop computer and a high-speed university-based internet connection. All patients used their own home computer, high speed internet connection, and a web camera to connect with the therapist. We reported that both interventions are equally effective in the treatment of tics and co-occurring disorders in children and adolescents affected by TS. Patients in both groups showed a reduction in the severity of tics, obsessive-compulsive symptoms, core-ADHD symptoms, and anxious symptoms, as assessed by the rating scales, at T1. Furthermore, no statistically significant differences were observed between the ftf-BT group vs. or-BT –group in the variation of the severity of these symptoms between T0 and T1. Conversely, between-group differences in clinician-rated severity of depressive symptoms did reach statistical significance (Prato et al., 2022). Considering the short follow-up period, the results of the previous study should be considered as preliminary rather than conclusive. The purpose of this prospective cohort study is to report the trajectory and course of illness after 6 months of follow-up of this originally reported sample, as well as their response to BT. We hypothesized that TS patients would improve similarly at 6-month follow-up with ftf-BT, but also with or-BT. We aimed to demonstrate that or-BT may represents a promising treatment option for patients with TS, likely beyond the end of the COVID-19 pandemic.

2. MATERIALS AND METHODS

2.1. Study design

This study was conducted at the Child and Adolescent Neurology and Psychiatry of the Medical and Experimental Department of Catania University. All 40 TS patients

previously reported in our pilot study were diagnosed by a team of paediatric neuropsychiatrists with solid experience in tic disorders and possible comorbidities according to the DSM-5 (APA, 2013), and were offered continuing care at our outpatient Tourette clinic for tics. We enrolled patients aged 9–16 years of age with a primary diagnosis of TS, that presented tics of moderate severity and an intelligence quotient (IQ) > 80. All parents gave written informed consent, and the subjects assented, when possible, for participation. Data collection was made in the context of a standardized research assessment and included demographic variables such as age and sex, a detailed information about the course and phenomenology of patients' tics, presence of comorbidities, overall treatment approaches in addition to BT.

2.2. Clinical assessment

Among the clinical cohort, modifications in symptoms severity were further evaluated after 6 months. At the initial consultation (T0), patients were assessed according to Yale Global Tic Severity Rating Scale (YGTSS), Premonitory Urge for Tic Scale (PUTS), Children's Yale-Brown Obsessive-Compulsive Scale for Children (CY-BOCS), Multidimensional Anxiety Scale for Children (MASC), Child Depression Inventory (CDI), and the Conners' Parent Rating Scale (CPRS). The clinical assessment was repeated in all patients at 2-month follow-up visit (T1) (Prato et al., 2022). After 6 months (T2), all participants were further examined for tics and potential associated comorbid disorders. The 6-month follow-up evaluation was made with the same instruments used at baseline and after two months (T1). At the 6-month assessment, modifications in symptoms severity were recorded by the difference in the YGTSS, CY-BOCS, PUTS,

CPRS, CDI and MASC scales. Those TS patients who manifested a decrease no less of 25% in YGTSS scores have been considered as “responders”.

2.3. Measures

The YGTSS is a clinician-rated scale used to assess the motor and phonic tic severity considering the number, frequency, duration, intensity, and complexity of tics. It consists of separate motor and vocal tic checklists scored from 0 to 5 on two subscales for motor and vocal tics. The subscales were combined to produce a total tic severity score (ranging from 0 to 50). Another score ranging from 0 to 50 was assigned for global impairment due to tics (Leckman et al., 1989). The PUTS measures sensory and mental phenomena associated with premonitory urges in 10 items on a four-point scale (range 10–40). The first 6 items include itchiness, energy, pressure, tense feeling, incomplete, or a not “just right” feeling before performing a tic. The additional 4 items assess whether these feelings are experienced almost all the time before a tic, if they happen with every tic, if they go away after the tic is performed, and if subjects can stop the tics for a short period of time (Woods et al., 2005). To evaluate OCD, commonly associated with tic disorders, the CY-BOCS, a semi-structured clinician administered interview assessing the severity of obsessions and compulsions occurring over the past week across five areas (time, interference, distressing nature, effort to resist, control over obsessions and compulsions) was also administered (Scahill et al., 1997). The CPRS is a useful tool for obtaining parental reports of childhood behavior problems that contains summary scales supporting ADHD diagnosis and quantifying ADHD severity (Conners, 1997). Finally, all participants completed the MASC, a self-report scale that robustly represents the factor structure of anxiety in children aged 8–18 years (March et al., 1997) and the Child Depression Inventory: a 27-item self-report instrument that assesses depressive symptoms in 7- to 17-year-olds (Kovacs, 1988).

2.4. Statistical Analysis

Clinical variables of patients are summarized using means and standard deviations (SD) for continuous data or count (%) for categorical data. We assessed the distribution of quantitative variables to determine their deviation from the normal distribution (Shapiro–Wilk test). Since the distribution of the rating scales was not normal, we assessed the time-points by non-parametric methods. Specifically, we computed the variation between the values at the two time points, first consultation (T0) and follow-up visit at 6 months (T2), in both groups separately. Clinical outcomes of YGTSS rating scales among T0 and T2 were also evaluated to discriminate responders' patients, who showed a reduction at least 25% in scores (Jeon et al., 2013). A series of 3×2 mixed-model analyses of variance (ANOVA) test were performed to examine interaction effect between intervention type and time (group x time), the main effects of time (T0, T1, T2), and group (ftf-BT or or-BT). ANOVA tests were separately conducted on the outcome variables obtained by computing the difference between the YGTSS, PUTS, CYBOCS, MASC, CDI, CPRS scores at baseline (T0), and the same scores at week 8 (T1) or week 24 (T2) among participants in ftf-BT group relative to or-BT group. Statistically significance for all analysis was set at the level of $p < 0.05$, and confidence intervals are given with 95% margin. Data were analysed using SPSS software (SPSS, Inc., Chicago, IL, USA, IBM, Somers, NY, USA).

3. RESULTS

3.1. Sample description

Participants of the or-BT group were more likely male (male = 90%, n=18) and presented a mean age of 13.3± 2.0 years old. The mean age of tic onset was 5.8 ± 1.0. Comorbid

OCD affected 60% (n=12), Anxiety 45% (n=9), and learning disabilities (LD) 40% (n=8). Nine (45%) received a pharmacological treatment (1 drug in 4, 2 drugs in 4, 3 drugs in 1) with no good response or a partial symptoms control. The most used treatments were atypical antipsychotics (45%, n=9) and selective serotonin reuptake inhibitors (SSRIs) (10%, n=2). Participants presented a mean IQ of 104.0 (± 9.3). The ftf-BT group includes predominantly males (male =90%, n=18). Participants of this group presented a mean age of 13.8± 2.0 years old, and a mean age of tic onset of 5.9 ± 1.4. Among the individuals of ftf-BT group, the most common comorbid psychiatric disorders were OCD (60%, n=12), LD (45%, n=9) and anxiety disorder (40%, n=8). Eight patients (40%) received a pharmacological treatment (1 drug in 5, 3 drugs in 3) with no good response or a partial symptoms control. The most used treatments were atypical antipsychotics (25%, n=5), neuroleptic drugs (15%, n=3) and SSRIs (15%, n=3). Participants presented a mean IQ of 103.6 (± 12.0). No statistically significant differences were observed between two groups based on participant's demographic and clinical features, as just reported in our previous study (Prato et al., 2022).

3.2. Efficacy of Group Intervention for Tic Severity and comorbid symptoms

The variations in rating scores are shown in Table 1-3. For the YGTSS total score, interaction was non-significant whereas time effect was significant. Total tics significantly decreased at 6-month follow-up visits in or-BT group (mean total decrease = 11.8 ±3.7 points, $p<0.001$) and in ftf-BT group (mean total decrease = 12.0 ± 2.4 points, $p < 0.001$). Notably, 100% (n=20) of patients of or-BT -group achieved at least 25% reduction in YGTSS scores from baseline (T0) at T2. Instead, the decrease of 25% in YGTSS ratings was detected in 85% (n=17) of patients of the ftf-BT group. Interaction,

time, and group effects regarding PUTS were non-significant for both groups across assessment points (all p's>0.05). While there was a similar decrease in PUTS from initial consultation to 6-month follow-up in both groups (mean total decrease = 0.15 ± 0.5 points, the detected change was not statistically significant (Table 1-3). For the CYBOCS total score, interaction was non-significant whereas time effect was significant. Patients of both groups also showed between the first visit and the follow-up visit after 6 months a significant variation in the severity of obsessive-compulsive symptoms, with a mean total reduction of 9.05 (SD 4.5) points in the or-BT group ($p < 0.001$), and a mean total decrease of 8.9 (SD 5.3) points in the ftf-BT group ($p < 0.001$) (Table 1-3). Notably, both treatment approaches were effective in reducing CYBOCS total scores, and this effect persisted over time. For the CDI, MASC and CPRS total scores, interaction was non-significant whereas time effect was significant. There was a significant improvement from T0 and T2 in depressive symptoms on the CDI in the or-BT group, with a mean total reduction of 3.35 (SD 0.1) points ($p< 0.001$), in anxiety symptoms, with a mean total decrease of 15.15 (SD 6.7) and on the MASC total score ($p<0.001$) (Table 1-3). Among the ftf-BT group, statistically significant improvements from T0 and T2 were observed in the variation of the severity of depressive symptoms on the CDI, with a mean total reduction of 2.35 (SD 0.1) points ($p< 0,001$), and in anxiety symptoms, with a mean total decrease of 16.8 (SD 6.8) on the MASC total score ($p< 0.001$) (Table 1-3). Finally, there was a significant improvement in CPRS total score from initial consultation to 6-month follow-up both in or-BT group ($p=0.0065$) and in ftf-BT group ($p=0.001$) (Table 1-3).

4. DISCUSSION

Several studies have already showed that DHIs could be an innovative and useful therapeutic approach to improving health care for patients affected by TS. Considering the time of COVID-19 pandemic and the reported barriers to the availability to BT, in

recent years there has been a renewed interest in the delivery of BT remotely. Two small pilot RCT studies have compared the efficacy of BT delivered remotely via videoconference to traditional face-to-face delivery in children with TS (Himle et al., 2012, Ricketts et al., 2016). Results of these studies showed comparably significant tic reduction for both groups, among the TS patients receiving CBIT via videoconference vs. the patients receiving face-to-face CBIT (Himle et al., 2012, Ricketts et al., 2016). Himle et al. (2012) found that tic severity was reduced regardless of the CBIT modality, with similar within-group effects at a 4-month follow-up (Himle et al., 2012). Another RCT conducted by Ricketts et al. (2016) found more significant reductions in clinician-rated and patient-reported tic severity among the 12 patients in the VoIP-delivered CBIT group after 10 weeks (Ricketts et al. 2016). In the study conducted by Himle et al. (2012), participants were still required to travel to local clinics to access the telehealth equipment, which negates some benefits of virtual delivery. Conversely, Ricketts et al. (2016) demonstrating that CBIT could be delivered in patients' homes using common, commercially available voice-over- Internet protocol (VOIP) platforms. Furthermore, participant's and their parents of both studies reported a good therapeutic relationship with the delivery modality of videoconferencing (Himle et al., 2012, Ricketts et al., 2016). However, although videoconferencing may solve the issue of long travel distances, it does not remedy the shortage of trained therapists, or the high costs associated with treatment. With the aim to increase availability of BT for young people with tic disorders, Andrén et al. (2019) developed two novel therapist-guided and parent-guided internet-delivered interventions based on existing HRT and ERP protocols in a small pilot study. Both interventions resulted in a significant reduction in tic-related impairment and parent-rated tic severity, but only BIP TIC ERP showed a significant improvement in clinician-rated tic severity, and the therapeutic gains were maintained at the 12-month follow-up (Andrén

et al., 2019). An additional advantage of this treatment format was that it demanded less therapist time (approximately an average of 25 min per participant per week, mainly via text messages) than traditional face-to-face BT. In a recent RCT Rachamim et al. (2020) compared internet delivered CBIT to a waitlist condition and demonstrated clinically meaningful reductions in tic severity and improved youth global impairment and functioning. Gains were maintained over a 6-month follow-up period (Rachamim et al., 2020). Instead, in another multicentre, parallel group, single-blind RCT, Hollis et al. (2021) evaluated the clinical effectiveness and costs of a therapist-supported, parent-assisted, internet-delivered ERP programme for tics in children and adolescents in England, and suggested that remotely delivered, online ERP with minimal therapist contact time could represented an efficient public mental health approach to improve access to BT for tics in children and adolescents (Hollis et al., 2021). Recently, another RCT conducted by Andrén et al. (2022b) investigated the effectiveness of therapist-supported online ERP treatment for children with TS and CTD compared with therapist-supported online education courses for tics (Andrén et al., 2022b). Both interventions were associated with clinically meaningful improvements in tic severity, but ERP led to higher response rates (47% vs 29%) at little additional cost. Previous studies regarding remote-BT conducted in paediatric TS patients are summarized in Table 4. Other research studies have also demonstrated the efficacy and safety of internet-delivered BT in the treatment of tics compared to ftf-BT for adults with tic disorders (Jakubovski et al., 2016; Haas et al., 2022). In particular, Haas et al. (2022) developed a completely therapist-independent internet-delivered platform to deliver CBIT (iCBT) for adult patients with tic disorders and suggested a clinically relevant tic reduction in adults with tics after iCBIT (Haas et al., 2022). Remarkably, treatment effects of iCBIT further increased after end of treatment over a 6-month follow-up period (Haas et al., 2022). In addition, a recent

single-arm trial demonstrated strong evidence of feasibility, acceptability, and preliminary effectiveness of tele-CBIT comparable to in-person treatment for both pediatric and adult patients with tic disorders (Capriotti et al., 2023). Overall, our data are in line with recent studies showing a significant tic reduction in children and adolescents with TS after using or-BT. The results of this trial show that or-BT and ftf-BT are both effective in reducing tic severity as measured by YGTSS scores. Moreover, this improvement persisted over time, at least until the end of the follow-up period (24 weeks). Our results are in line with data from the literature which have highlighted the efficacy of BT remotely in the treatment of tic disorders. However, compared to other studies, we found at 6-month follow-up visit a higher improvement in both groups after treatment with no between-group differences assessed by YGTSS (13.7 in the or-BT -group, 13,8 in the ftf-BT -group) (Table 4). Overall, the results of the current study indicate that non-inferiority of or-BT in comparison to ftf-BT for children and adolescents with tics. However, the results should be considered preliminary, considering the limitations of this study, which consisted of a small sample. Considering the waxing-waning time course of tic disorders, length of follow-up is an important point. Evaluation of long-term outcomes after treatment with BT remotely is lacking, making it difficult to draw definitive conclusions on the efficacy of BT through videoconference for the treatment of tics in patients with tic disorders. It is noteworthy that in this trial we investigate the impact of treatment not only for tics, but also for complex comorbid conditions. The result suggests a positive treatment response in both groups, with a significantly improvement of obsessive-compulsive symptoms, anxiety, depressive and ADHD-core symptoms, as assessed by neuropsychological findings at baseline and at follow-up visits. Gains were maintained over a 6-month follow-up period. Statistically significant improvements were reached in both treatment group in all concomitant symptoms assessed through rating

scales, except for premonitory urge (PU) as evaluated by PUTS. PUs is unpleasant sensory phenomena that play a crucial role in triggering tics. TS participants of both groups showed a reduction of PUTS scores, at 6-month- follow-up visit, but this variation did not reach a statistical significance. Instead, the suitability of the PUTS for younger children has not yet been established, even though PUs may already be present at a young age (Openneer et al., 2020). To date, no more studies have examined the evolution and characteristics of comorbid conditions after treatment over telehealth. A recent RCT conducted by Rachamim et al. (2021) showed that internet-based self-help CBIT (ICBIT) for children and teens supported by their parents and with minimal remote therapist intervention was also effective in the presence of comorbid ADHD or OCD symptomatology and may reduce symptoms of inattention and impulsivity (Rachamim et al., 2021). Overall, these positive results are promising, but larger studies should examine with more details the outcome non only of tics but also associated comorbidities after these treatment approaches. The current study has several limitations that warrant mention. First, the small-sample size limited statistical power, which in turn limited the number of exploratory analyses that could be conducted. Second, longer-term follow-up assessment was not included, so maintenance of gains cannot be reported. Third, the study did not include a non-BT control group. Also, it would be helpful to explore a combination of both variants of treatments, to compare their respective therapeutic effects. In addition, there were many patients who received some form of adjunctive intervention, that might also influence tic improvement. Moreover, the influence of the comorbid conditions was not full analysed. Collectively, these limitations limit generalizability of the results.

5. CONCLUSIONS

This research study suggest that or-BT is a promising and effective tool in the treatment of tics and co-occurring disorders in children and adolescents affected by tic disorders. Although the benefits of offering BT remotely for individuals with TS have been reported, long-term studies are required to compare this alternative treatment option to traditional face-to-face care. It would also be informative to explore relationships between or-BT and therapeutic outcomes, including not only tics but also the wide spectrum of possible presented comorbidities.

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Table 1 - Yale global Tic severity rating scale (YGTSS), Premonitory Urge for Tic Scale (PUTS), Children's Yale-brown obsessive-compulsive scale for children (CY-BOCS), Multidimensional anxiety scale for children (MASC), child depression inventory (CDI) outcome in patients of the or-BT group.

or – BT group	Mean change	Confidence Interval, 95%	p-value
YGTSS total score	11.8 (SD 3,7)	[-14.59, -9.01]	<0.001*
PUTS total score	0.15 (SD 0.5)	[-0.6124, 0.3124]	0.5054
CYBOCS total score	9.05 (SD 4.5)	[-12.6352, -5.4648]	<0.001*
MASC total score	15.15 (SD 6.7)	[-19.4954, -10.7046]	<0.001*
CDI total score	3.35 (SD 0.1)	[-4.2123, -2.3877]	<0.001*
CPRS total score	8.9 (SD 8.5)	[-14.9148, -2.7852]	0,0065*

Table 2 - Yale global Tic severity rating scale (YGTSS), Premonitory Urge for Tic Scale (PUTS), Children's Yale-brown obsessive-compulsive scale for children (CY-BOCS), Multidimensional anxiety scale for children (MASC), child depression inventory (CDI) outcome in patients of the ftf-BT group.

ftf - BT group	Mean change	Confidence Interval, 95%	p-value
YGTSS total score	12.0 (SD 2.4)	[-15.1513, -8.7487]	<0.001*
PUTS total score	0.15 (0.5)	[-0.9283, 0.6283]	0,6912
CYBOCS total score	8.9 (5.3)	[-12.9599, -4.8401]	<0.001*
MASC total score	16.8 (SD 8.8)	[-23.1705, -10.3295]	<0.001*
CDI total score	2.35 (SD 1.0)	[-3.0504, -1.6496]	<0.001*
CPRS total score	7.55 (SD 6.2)	[-11.5446, -3.4554]	0,001*

Table 3 - Tics severity and comorbid symptoms on key outcome measures at baseline (T0) and post-intervention (T1, T2) by group.

Measures	Time	or - BT - Mean (SD)	ftf - BT - Mean (SD)	Time effect (p)	Group effect (p)	Interaction (p)
YGTSS total score	0	25.5 (SD 10.5)	25.8 (SD 7.3)	<0,0001*	0.9176	0.965
	1	14.1 (SD 6.3)	13.7 (SD 5.4)			
	2	13.7 (SD 6.8)	13.8 (SD 4.9)			
PUTS total score	0	13.55 (SD 2.9)	13.1 (SD 2.3)	0,825	0.470	1
	1	13.51 (SD 3.2)	13.1 (SD 2.6)			
	2	13.4 (SD 3.4)	12.95 (SD 2.8)			
CYBOCS total score	0	22.3 (SD 12.0)	22.7 (SD 12.7)	<0,0001*	0.83	0.973
	1	14.3 (SD 6.6)	15.1 (SD 7.2)			
	2	13.25 (SD 7.5)	13.8 (SD 7.4)			
MASC total score	0	35.1 (SD 16.8)	36.2 (SD 15.3)	<0,0001*	0.9009	0.709
	1	21.6 (SD 10.1)	22.6 (SD 5.4)			
	2	19.95 (SD 10.1)	19.4 (SD 6.5)			
CDI total score	0	4.5 (SD 1.9)	4.3 (SD 2.6)	<0,0001*	0.5046	0.331
	1	3.4 (SD 1.6)	4.3 (SD 2.5)			
	2	1.15 (SD 1.8)	1.95 (SD 1.6)			
CPRS total score	0	21.2 (SD 22.4)	20.2 (SD 17.2)	0,031*	0.9324	0.8603
	1	14.3 (SD 11.7)	14.7 (SD 9.5)			
	2	12.3 (SD 13.9)	12.65 (SD 11.0)			

Table 4 –Summary of studies on online-remote BT in paediatric TS patients.

Study	Design	Interventions	Participants (n^o)	Follow-up	Results
Himle et al. (2012)	RCT	ICBT, F2F CBT	18	4 months	ICBT: 7.8 points reduction FCBT: 6.5 points reduction
Ricketts et al. (2016)	RCT	ICBT, WL	20	10 weeks	ICBIT>WL ICBIT: 25.75 to 18.50 WL: 22.0 to 20.25
Andrén et al. (2019)	RCT	BIP TIC HRT, BIP TIC ERP	23	12 months	BIP TIC HRT: 23.75 to 19.00 BIP TIC ERP: 23.45 to 21.18
Rachamim et al. (2020)	RCT	ICBIT, WL	41	6 months	ICBIT: 22.72.58 to 16.12 WL: 21.88 to 20.94
Hollis et al. (ORBIT) (2021)	RCT	BIP TIC ERP, PE	224	3 months	BIP TIC ERP: 28.4 to 21.5 PE: 28.4 to 25.0
Andrén et al. (2022)	RCT	BIP TIC ERP, PE	221	3 months	BIP TIC ERP: 23.0 to 17.0 PE: 24.0 to 19.0
This study (2023)	RCT	Or-BT, ftf-BT	40	6 months	or-BT: 25.5 to 13.7 Ftf-BT: 25.8 to 13.8